

IN THE PIPELINE

Updates on Promising Agents in Development for Gastroenterology & Hepatology

FDA Approves Simeprevir for Treatment of Hepatitis C Virus Infection

Simeprevir (Janssen), to be marketed as Olysio, was approved by the US Food and Drug Administration (FDA) for use in combination with pegylated interferon and ribavirin in the treatment of genotype 1 chronic hepatitis C virus (HCV) infection in adults with compensated liver disease, including cirrhosis. The decision was made on November 23, 2013. Simeprevir, given once daily at a dose of 150 mg, is now the third protease inhibitor to be approved for use in the treatment of HCV infection.

The New Drug Application (NDA) for simeprevir was based on 3 pivotal phase 3 studies—QUEST-1 and QUEST-2, which studied the agent in treatment-naïve patients, and PROMISE, which studied the agent in patients who relapsed after interferon-based treatment—and the phase 2b ASPIRE study, which studied the agent in prior nonresponder patients.

FDA Antiviral Advisory Committee Recommends Approval of Sofosbuvir

In a 15 to 0 vote, the Antiviral Drugs Advisory Committee of the FDA unanimously recommended approval of sofosbuvir (Gilead Sciences) in combination with ribavirin for the treatment of adults chronically infected with genotype 2 or 3 HCV. The committee also unanimously recommended approval of sofosbuvir in combination with pegylated interferon and ribavirin in treatment-naïve adults chronically infected with genotype 1 or 4 HCV. The target date for the official decision of sofosbuvir's NDA, which was submitted in April 2013, is December 8, 2013.

Sofosbuvir is a direct-acting nucleotide analogue inhibitor of the HCV nonstructural (NS) 5B polymerase enzyme, which plays a role in HCV replication. The NDA for the agent is supported by data from 5 phase 3 studies—NEUTRINO, FISSION, POSITRON, FUSION, and VALENCE—in which 12 or 16 weeks of sofosbuvir-based therapy was found to be either superior or noninferior to currently available treatments based on the propor-

tion of patients who had a sustained virologic response at 12 weeks after completing therapy.

Janssen Expands Pipeline with the Acquisition of NS5A Inhibitor GSK2336805

Janssen Pharmaceuticals has acquired the rights to develop and market the investigational direct-acting antiviral GSK2336805 from GlaxoSmithKline. GSK2336805 is a once-daily oral NS5A replication complex inhibitor under study for interferon-free regimens in the treatment of HCV infection. Janssen intends to launch phase 2 studies of GSK2336805 in combination with the NS3/4A protease inhibitor simeprevir and nonnucleoside polymerase inhibitor TMC647055 as an interferon-free regimen for chronic HCV infection in adults with compensated liver disease.

Protease Inhibitor/NS5A Inhibitor Granted Breakthrough Therapy Designation

Two investigational drugs in the Merck pipeline were granted Breakthrough Therapy designation by the FDA for treatment of chronic HCV infection. MK-5172 is an NS3/4A protease inhibitor, and MK-8742 is an NS5A replication complex inhibitor. The MK-5172/MK-8742 oral combination is in phase 2 trials for treatment of genotype 1 HCV infection. Support for the Breakthrough Therapy designation included interim results of the phase 2b C-WORTHY study, reported at the annual scientific meeting of the American Association for the Study of Liver Diseases (AASLD), which took place on November 1 to 5, 2013 in Washington, DC. Eric Lawitz, MD, of the University of Texas Health Science Center and the Texas Liver Institute in San Antonio, who presented the interim C-WORTHY results, reported that MK-5172/MK-8742 with or without ribavirin was associated with robust virologic suppression in treatment-naïve, noncirrhotic patients with genotype 1 HCV infection. Read more on this study in Highlights From AASLD 2013 in this issue of *Gastroenterology & Hepatology*.